WE CLAIM:

1. A contrast agent for diagnostic imaging comprising:

a) an image-enhancing moiety (IEM);

b) a plasma protein binding moiety (PPBM); and

c) a blood half-life extending moiety (BHEM),

the contrast agent demonstrating at least about 10% binding to plasma proteins and, in a rat plasma pharmacokinetic experiment, an area under the plasma concentration versus time curve from 0 to 10 minutes which is at least about 20% greater than that observed for the combination of the IEM and the PPBM alone without the BHEM.

2. The contrast agent according to claim 1, wherein the image-enhancing moiety is selected from the group consisting of organic molecules, metal ions, salts or chelates, particles, iron particles, or labeled peptides, proteins, polymers or liposomes.

3. The contrast agent according to claim 1, wherein the image-enhancing moiety is a physiologically compatible iron particle or metal chelate compound consisting of one or more cyclic or acyclic organic chelating agents complexed to one or more paramagnetic metal ions with atomic numbers 21-29, 42, 44, or 57-83.

4. The contrast agent according to claim 1, wherein th image-enhancing moiety is an iodinated organic molecule or a physiologically compatible metal chelate compound consisting of one or more cyclic or

acyclic organic chelating agents complexed to one or more metal ions with atomic numbers 57 to 83.

5. The contrast agent according to claim 1, wherein the image-enhancing moiety is gas-filled bubbles or particles or a physiologically compatible metal chelate compound consisting of one or more cyclic or acyclic organic chelating agents complexed to one or more metal ions with atomic numbers 21-29, 42, 44, or 57-83.

6. The contrast agent according to claim 1, wherein the image-enhancing moiety consists of a radioactive molecule.

7. The contrast agent according to claim 1, wherein the image-enhancing moiety is a physiologically compatible metal chelate compound consisting of one or more cyclic or acyclic organic chelating agents complexed to one or more metal ions with atomic numbers 27, 29, 31, 43, 47, 49, 75, 79, 82 or 83.

8. The contrast agent according to claim 1, wherein the image-enhancing moiety is a physiologically compatible metal chelate compound consisting of one or more cyclic or acyclic organic chelating agents complexed to Tc-99m.

9. The contrast agent according to claim 1, wherein the image-enhancing moiety is an organic or inorganic dye.

10. The contrast agent according to claim 1, wherein the plasma protein binding moiety binds to human serum albumin.

11. The contrast agent according to claim 10, wherein the plasma protein binding moiety comprises an aliphatic group and/or at least one aryl ring.

12. The contrast agent according to claim 10, wherein the plasma protein binding moiety comprises a peptide containing hydrophobic amino acid residues and/or substituents with or without hydrophobic or hydrophilic termination groups.

13. The contrast agent according to claim 10, wherein the plasma protein binding moiety contains at least one aryl ring.

14. The contrast agent according to claim 10, wherein the plasma protein binding moiety contains at least two aryl rings held rigidly in a non-planar fashion.

15. The contrast agent according to claim 1, wherein the blood half-life extending moiety possesses one or more full or partial negative charges in aqueous solution at physiological pH wherein the negative charge cannot be partially or fully neutralized by covalent or coordinate covalent bonding to the image-enhancing moiety.

16. The contrast agent according to claim 1, wherein the contrast agent demonstrates at least about 50% binding to plasma proteins.

17. The contrast agent according to claim 1, wherein the contrast agent demonstrates at least about 80% binding to plasma proteins.

18. The contrast agent according to claim 1, wherein the contrast agent demonstrates at least about 95% binding to plasma proteins.

19. The contrast agent according to claims 1, 16, 17 or 18, wherein the contrast agent demonstrates, in a rat plasma pharmacokinetic experiment, an area under the plasma concentration versus time curve from 0 to 10 minutes which is at least about 40% greater than that observed for the combination of the IEM and the PPBM alone without the BHEM.

20. The contrast agent according to claims 1, 16, 17 or 18, wherein the contrast agent demonstrates, in a rat plasma pharmacokinetic experiment, an area under the plasma concentration versus time curve from 0 to 10 minutes which is at least about 70% greater than that observed for the combination of the IEM and the PPBM alone without the BHEM.

21. The contrast agent according to claims 1, 16, 17 or 18, wherein the contrast agent

demonstrates, in a rat plasma pharmacokinetic experiment, an area under the plasma concentration versus time curve from 0 to 10 minutes which is at least about 100% greater than that observed for the combination of the IEM and the PPBM alone without the BHEM.

22. The contrast agent according to claims 1, 16, 17 or 18, wherein the contrast agent demonstrates, in a rat plasma pharmacokinetic experiment, an area under the plasma concentration versus time curve from 0 to 10 minutes which is from about 20% to about 100% greater than that observed for the combination of the IEM and the PPBM alone without the BHEM.

23. The contrast agent according to claims 1, 16, 17 or 18, wherein the contrast agent demonstrates, in a rat plasma pharmacokinetic experiment, an area under the plasma concentration versus time curve from 0 to 10 minutes which is from about 40% to about 100% greater than that observed for the combination of the IEM and the PPBM alone without the BHEM.

24. The contrast agent according to claims 1, 16, 17 or 18, wherein the contrast agent demonstrates, in a rat plasma pharmacokinetic experiment, an area under the plasma concentration versus time curve from 0 to 10 minutes which is from about 70% to about 100% greater than that observed for

the combination of the IEM and the PPBM alone without the BHEM.

25. The contrast agent according to claims 1, 16, 17 or 18, wherein the contrast agent demonstrates, in a rat plasma pharmacokinetic experiment, an area under the plasma concentration versus time curve from 0 to 10 minutes which is at least about 100% greater than that observed for the combination of the IEM and the PPBM alone without the BHEM.

26. The contrast agent according to claims 1, 16, 17 or 18, further comprising a targeting moiety which allows the contrast agent to target a selected biological component.

27. The contrast agent according to claim 26, wherein the targeting moiety is selected from the group consisting of lipophilic substances, receptor ligands, and antibodies.

28. A method for extending blood half-life of a diagnostic imaging contrast agent which comprises an image-enhancing moiety and a plasma protein binding moiety and demonstrates at least about 10% binding to plasma proteins, comprising the step of incorporating into the contrast agent a blood half-life extending moiety in a position within the agent such that it does not reduce the contrast agent's binding to plasma and such that the agent demonstrates, in a rat plasma pharmacokinetic experiment, an area under the plasma

concentration versus time curve from 0 to 10 minutes which is at least about 20% greater than that observed for the combination of the image-enhancing moiety and the protein plasma binding moiety alone without the blood half-life extending moiety.

29. The method according to claim 28, wherein the blood half-life extending moiety possesses one or more full or partial negative charges in aqueous solution at physiological pH and wherein the negative charge or charges cannot be partially or fully neutralized by covalent or coordinate covalent bonding to the image-enhancing moiety.

30. The method according to claim 28, wherein the area under the plasma concentration versus time curve from 0 to 10 minutes of the contrast agent is at least about 40% greater than that observed for the combination of the image-enhancing moiety and the protein plasma binding moiety alone without the blood half-life extending moiety.

31. The method according to claim 28, wherein the area under the plasma concentration versus time curve from 0 to 10 minutes of the contrast agent is at least about 70% greater than that observed for the combination of the image-enhancing moiety and the protein plasma binding moiety alone without the blood half-life extending moiety.

32. The method according to claim 28, wherein the area under the plasma concentration versus

time curve from 0 to 10 minutes of the contrast agent is at least about 100% greater than that observed for the combination of the image-enhancing moiety and the protein plasma binding moiety alone without the blood half-life extending moiety.

33. The method according to claim 28, wherein the area under the plasma concentration versus time curve of the contrast agent is from about 20% to about 100% greater than that observed for the combination of the image-enhancing moiety and the protein plasma binding moiety alone without the blood half-life extending moiety.

34. The method according to claim 28, wherein the area under the plasma concentration versus time curve of the contrast agent is from about 40% to about 100% greater than that observed for the combination of the image-enhancing moiety and the protein plasma binding moiety alone without the blood half-life extending moiety.

35. The method according to claim 28, wherein the area under the plasma concentration versus time curve of the contrast agent is from about 70% to about 100% greater than that observed for the combination of the image-enhancing moiety and the protein plasma binding moiety alone without the blood half-life extending moiety.

36. The method according to claim 28, wherein the area under the plasma concentration versus

time curve from 0 to 10 minutes of the contrast agent is at least about 100% greater than that observed for the combination of the image-enhancing moiety and the protein plasma binding moiety alone without the blood half-life extending moiety.

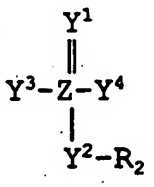
37. A diagnostic imaging contrast agent comprising the following formula:

$$IEM - [\ (L)_m - \{(BHEM)_s - (PPBM)_o\ \}_p\ ]_q$$

wherein IEM is an image-enhancing moiety,

L is a linker moiety,

BHEM is a blood half-life extending moiety possessing two or more electropositive hydrogen atoms, or two or more lone electron pairs that cannot be partially or fully neutralized by covalent or coordinate covalent bonding to the IEM, and is selected from the group consisting of sulfone, urea, thio-urea, amine, sulfonamide, carbamate, peptide, ester, carbonate, acetals and



or ester forms,

where Z = P, W, Mo, or S

Y^1, Y^2 = O or S

Y^3, Y^4 = O, S or not present

R_2 = H, C_{1-6} alkyl or not present,

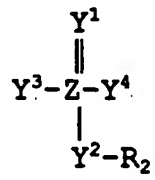
PPBM is a plasma protein binding moiety comprising at least seven carbon atoms,

m can be equal to 0-4,

s, o, and p can be the same or different and equal to 1-4,

and q is at least one.

38. The contrast agent according to claim 37, wherein the BHEM is



or ester forms,

where Z = P, W, Mo, or S

Y^1, Y^2 = O or S

Y^3, Y^4 = O, S or not present

R_2 = H, C_{1-6} alkyl or not present.

39. The contrast agent according to claim 37, wherein the BHEM is phosphate or ester forms thereof.

40. The contrast agent according to claim 37, wherein the PPBM comprises at least 13 carbon atoms.

41. The contrast agent according to claim 37, wherein the PPBM comprises at least 18 carbon atoms.

42. The contrast agent according to claim 37, wherein the PPBM has a log P contribution of at least 2.0.

43. The contrast agent according to claim 37, wherein the PPBM has a log P contribution of at least 3.0.

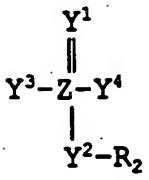
44. The contrast agent according to claim 37, wherein the PPBM has a log P contribution of at least 4.0.

45. A diagnostic imaging contrast agent comprising the following formula:

$$IEM - [\ (PPBM)_o \mid (BHEM)_s\ ]_r$$

wherein IEM is an image-enhancing moiety,

BHEM is a blood half-life extending moiety possessing two or more electropositive hydrogen atoms, or two or more lone electron pairs that cannot be partially or fully neutralized by covalent or coordinate covalent bonding to the IEM, and is selected from the group consisting of sulfone, urea, thio-urea, amine, sulfonamide, carbamate, peptide, ester, carbonate, acetals and



or ester forms,

where Z = P, W, or Mo

Y^1, Y^2 = O or S

Y^3, Y^4 = O, S or not present

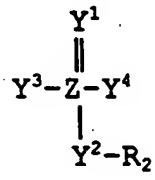
R_2 = H, C_{1-6} alkyl or not present,

PPBM is a plasma protein binding moiety comprising at least seven carbon atoms,

s and o can be the same or different and equal to 1-4,

and r is at least one.

46. The contrast agent according to claim 45, wherein the BHEM is



or ester forms,

where Z = P, W, or Mo

Y^1, Y^2 = O or S

Y^3, Y^4 = O, S or not present

R_2 = H, C_{1-6} alkyl or not present.

47. The contrast ag nt according to claim 45, wherein the BHEM is phosphate or ester forms thereof.

48. The contrast agent according to claim 45, wherein the PPBM comprises at least 13 carbon atoms.

49. The contrast agent according to claim 45, wherein the PPBM comprises at least 18 carbon atoms.

50. The contrast agent according to claim 45, wherein the PPBM has a log P contribution of at least 2.0.

51. The contrast agent according to claim 45, wherein the PPBM has a log P contribution of at least 3.0.

52. The contrast agent according to claim 45, wherein the PPBM has a log P contribution of at least 4.0.

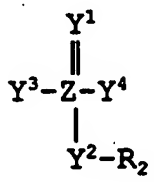
53. A diagnostic imaging contrast agent comprising the following formula:

$$\begin{array}{l} IEM - (PPBM)_o \\ \quad | \\ (L)_m - (BHEM)_s \end{array}$$

wherein IEM is an image-enhancing moiety,

L is a linker moiety,

BHEM is a blood half-life extending moiety possessing two or more electropositive hydrogen atoms, or two or more lone electron pairs that cannot be partially or fully neutralized by covalent or coordinate covalent bonding to the IEM, and is selected from the group consisting of sulfone, urea, thio-urea, amine, sulfonamide, carbamate, peptide, ester, carbonate, acetals, SO_3^- or ester forms and



or ester forms,

where Z = P, W, Mo, or S

Y^1, Y^2 = O or S

Y^3, Y^4 = O, S or not present

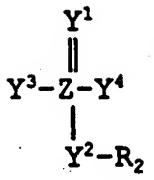
R_2 = H, C_{1-6} alkyl or not present,

PPBM is a plasma protein binding moiety comprising at least seven carbon atoms,

m can be equal to 0-4,

s and o can be the same or different and equal to 1-4.

54. The contrast agent according to claim 53, wherein the BHEM is



or ester forms,

where Z = P, W, Mo, or S

Y^1, Y^2 = O or S

Y^3, Y^4 = O, S or not present

R_2 = H, C_{1-6} alkyl or not present.

55. The contrast agent according to claim 53, wherein the BHEM is phosphate or ester forms thereof.

56. The contrast agent according to claim 53, wherein the PPBM comprises at least 13 carbon atoms.

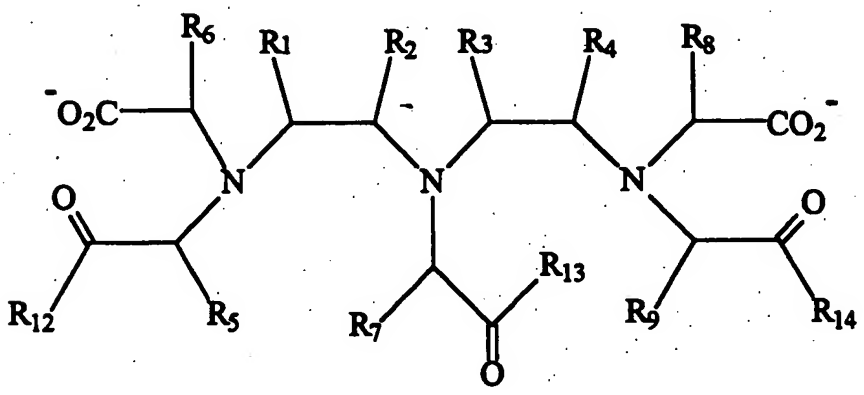
57. The contrast agent according to claim 53, wherein the PPBM comprises at least 18 carbon atoms.

58. The contrast agent according to claim 53, wherein the PPBM has a log P contribution of at least 2.0.

59. The contrast agent according to claim 53, wherein the PPBM has a log P contribution of at least 3.0.

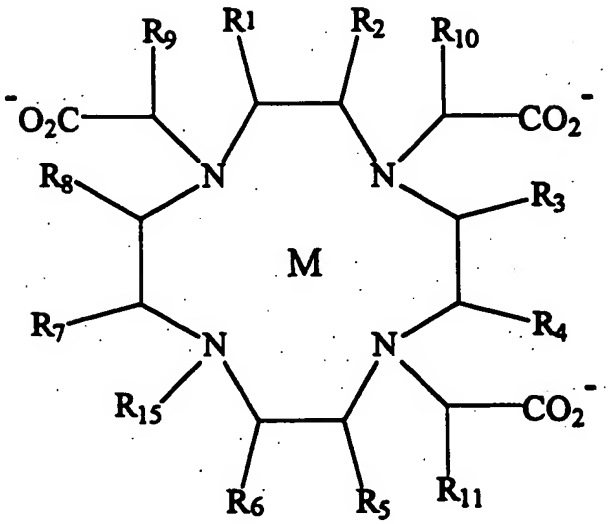
60. The contrast agent according to claim 53, wherein the PPBM has a log P contribution of at least 4.0.

61. A diagnostic imaging contrast agent comprising:



M

or



wherein M is a metal ion with an atomic number of 21-29, 42, 44 or 57-83,

R_1-R_{11} and R_{16} can be the same or different and selected from the group consisting of H, PPBM, BHEM and C_{1-6} alkyl,

provided that at least one of R_1-R_{11} or R_{16} is PPBM,

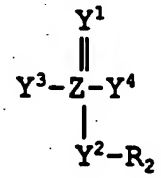
also provided that at least one of R_1-R_{11} or R_{16} is BHEM,

R_{12}, R_{13} and R_{14} can be the same or different and selected from the group consisting of O^- and $N(H)R_{17}$,

R_{15} = H, $CH_2CH(OH)CH_3$, hydroxy alkyl or $CH(R_{16})COR_{12}$,

R_{17} = H or C_{1-6} alkyl,

BHEM is a blood half-life extending moiety possessing two or more electropositive hydrogen atoms, or two or more lone electron pairs that cannot be partially or fully neutralized by covalent or coordinate covalent bonding to the IEM, and is selected from the group consisting of sulfone, urea, thio-urea, amine, sulfonamide, carbamate, peptide, ester, carbonate, acetals, COO^- or ester forms, SO_3^- or ester forms and



or ester forms,

where Z = P, W, Mo, or S

Y^1, Y^2 = O or S

Y^3, Y^4 = O, S or not present

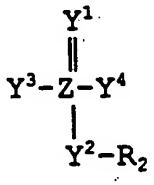
R_2 = H, C_{1-6} alkyl or not present,

PPBM is a plasma protein binding moiety comprising at least seven carbon atoms.

62. The contrast agent according to claim 61, wherein M is selected from the group consisting of Gd(III), Fe(III), Mn(II), Mn(III), Cr(III), Cu(II), Dy(III), Tb(III), Ho(III), Er(III) and Eu(III).

63. The contrast agent according to claim 62, wherein M is Gd(III).

64. The contrast agent according to any one of claims 61-63, wherein the BHEM is selected from the group consisting of COO^- or ester forms, SO_3^- or ester forms and



or ester forms,

where Z = P, W, Mo, or S
Y^1, Y^2 = O or S
Y^3, Y^4 = O, S or not present
R_2 = H, C_{1-6} alkyl or not present.

65. The contrast agent according to any on of claims 61-63, wherein the PPBM comprises at least 13 carbon atoms.

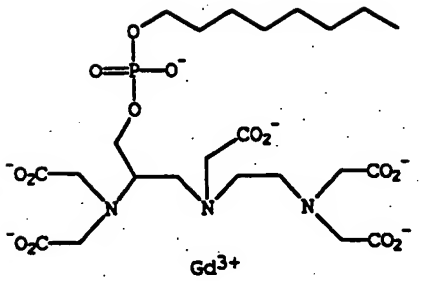
66. The contrast agent according to any one of claims 61-63, wherein the PPBM comprises at least 18 carbon atoms.

67. The contrast agent according to any one of claims 61-63, wherein the PPBM has a log P contribution of at least 2.0.

68. The contrast agent according to any one of claims 61-63, wherein the PPBM has a log P contribution of at least 3.0.

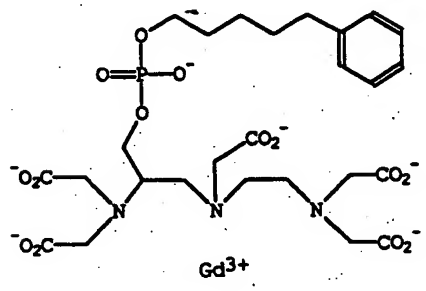
69. The contrast agent according to any one of claims 61-63, wherein the PPBM has a log P contribution of at least 4.0.

70. A compound having the formula:



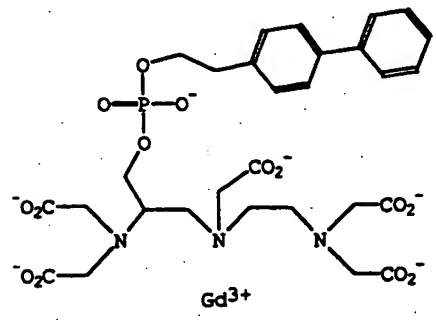
MS-315

71. A compound having the formula:



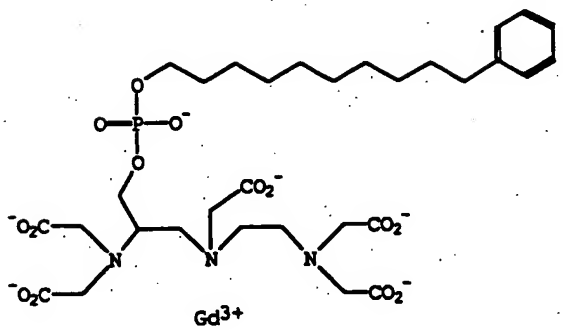
MS-317

72. A compound having the formula:



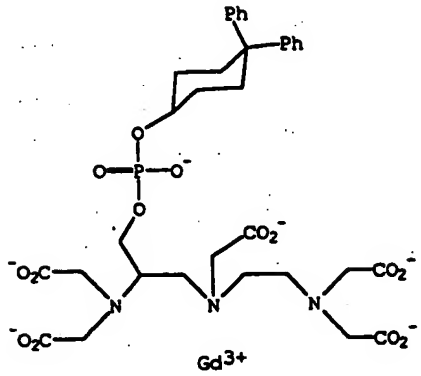
MS-322

73. A compound having the formula:



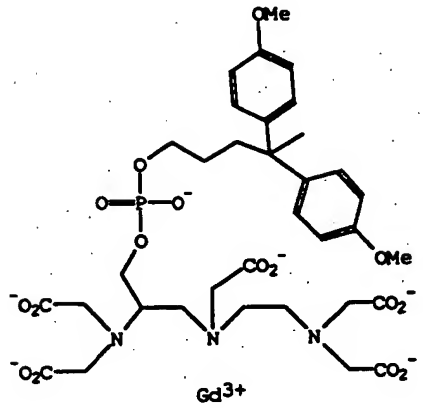
MS-323

74. A compound having the formula:



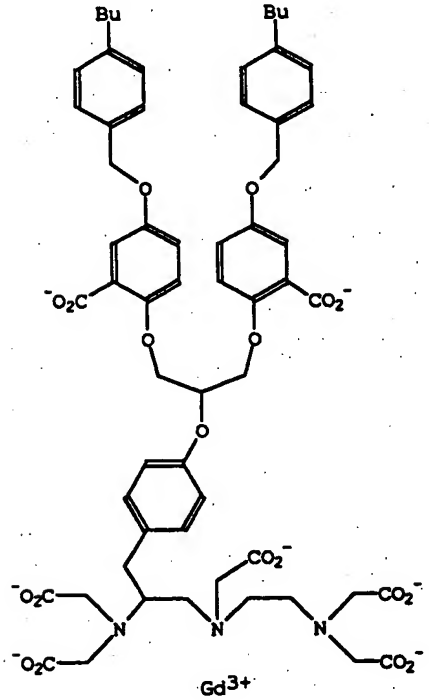
MS-325

75. A compound having the formula:

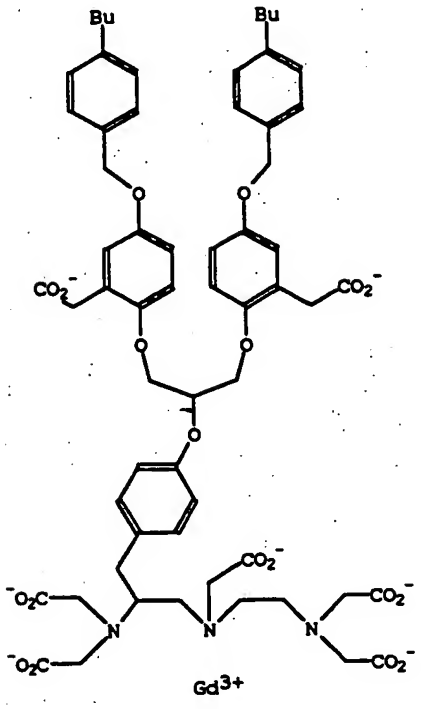


MS-328

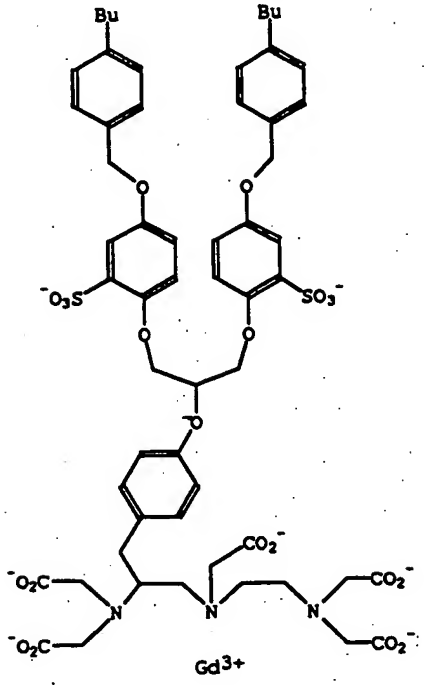
76. A compound having the formula:



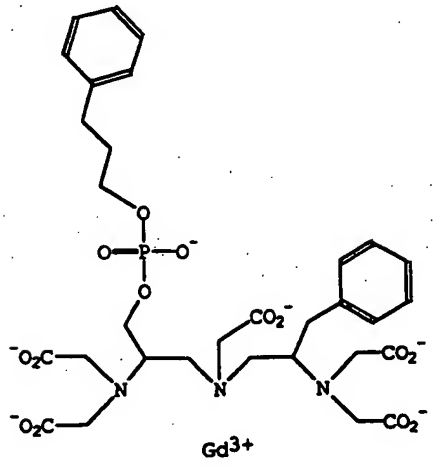
77. A compound having the formula:



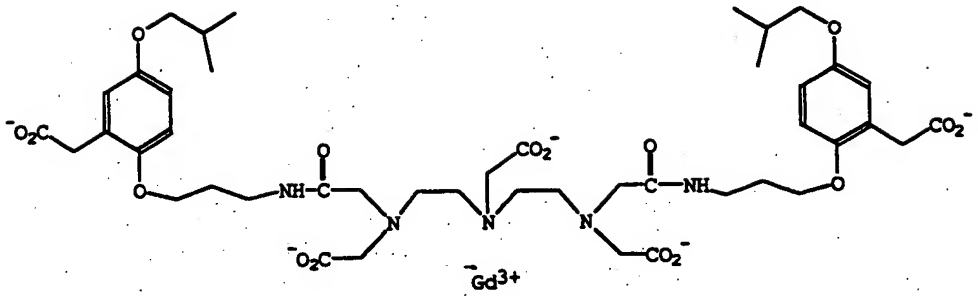
78. A compound having the formula:



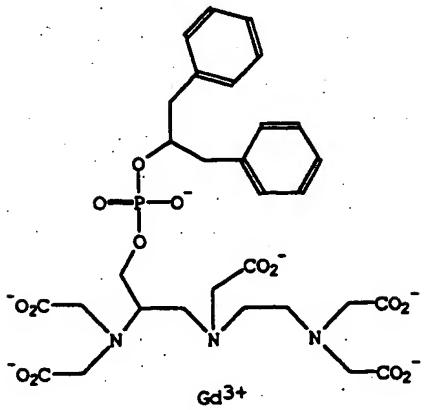
79. A compound having the formula:



80. A compound having the formula:

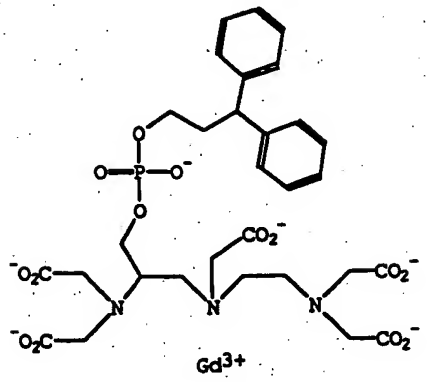


81. A compound having the formula:



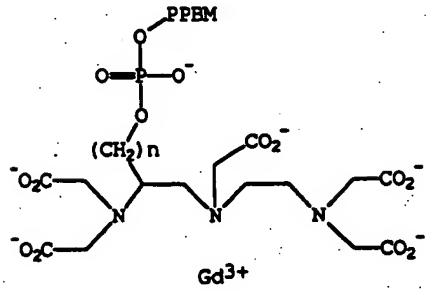
MS-326

82. A compound having the formula:



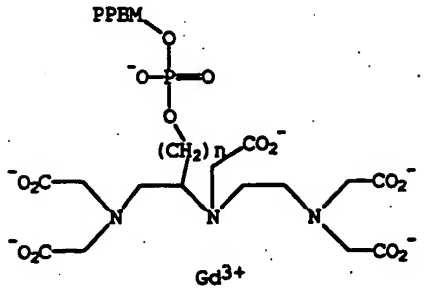
MS-327

83. A compound having the formula:



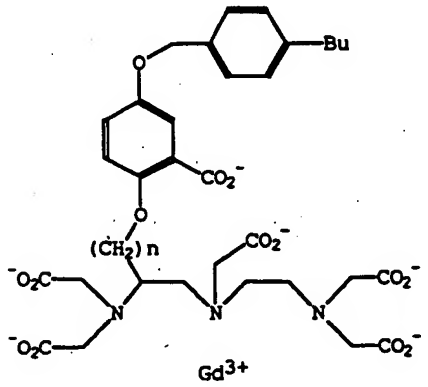
wherein PPBM is a plasma protein binding moiety comprising at least seven carbon atoms, and n can be equal to 1-4.

84. A compound having the formula:



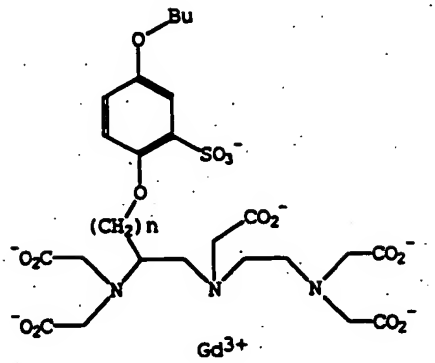
wherein PPBM is a plasma protein binding moiety comprising at least seven carbon atoms, and n can be equal to 1-4.

85. A compound having the formula:



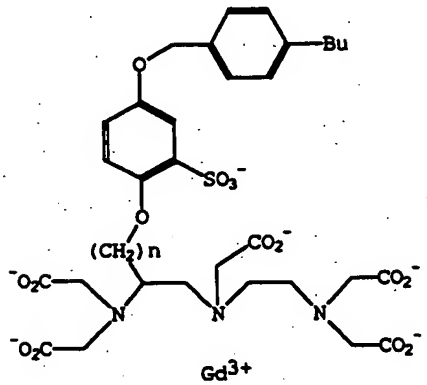
wherein n can be equal to 1-4.

86. A compound having the formula:



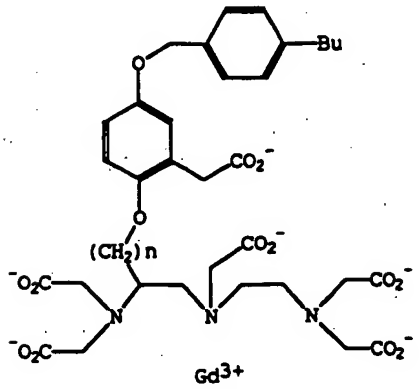
wherein n can be equal to 1-4.

87. A compound having the formula:



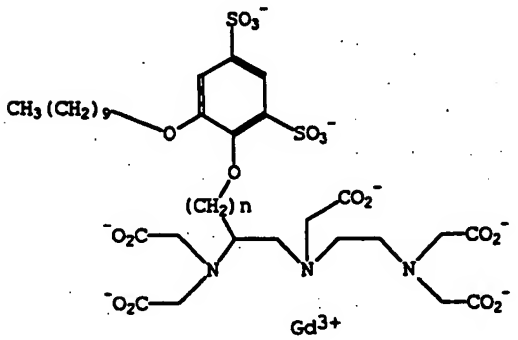
wherein n can be equal to 1-4.

88. A compound having the formula:



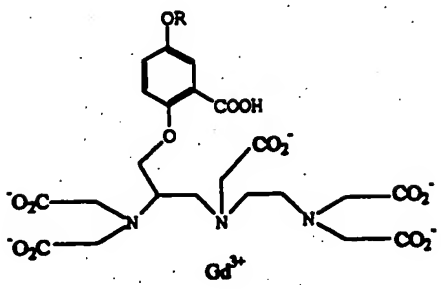
wherein n can be equal to 1-4.

89. A compound having the formula:



wherein n can be equal to 1-4.

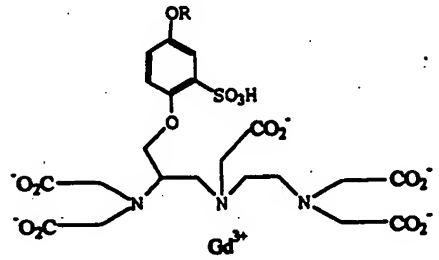
90. A compound having the formula:



wherein R comprises an aliphatic group and/or at least 1 aryl ring.

91. The compound according to claim 90, wherein R comprises a peptide containing hydrophobic amino acid residues and/or substituents with or without hydrophobic or hydrophilic termination groups.

92. A compound having the formula:



wherein R comprises an aliphatic group and/or at least 1 aryl ring.

93. The compound according to claim 92, wherein R comprises a peptide containing hydrophobic amino acid residues and/or substituents with or without hydrophobic or hydrophilic termination groups.

94. A method for MRI imaging of a biological component comprising the step of administering a diagnostically effective amount of a contrast agent according to any one of claims 1, 37, 45, 53 or 61.

95. A method for ultrasound imaging of a biological component comprising the step of administering a diagnostically effective amount of a contrast agent according to any one of claims 1, 37, 45, 53 or 61.

96. A method for x-ray imaging of a biological component comprising the step of administering a diagnostically effective amount of a contrast agent according to any one of claims 1, 37, 45, 53 or 61.

97. A method for nuclear radiopharmaceutical imaging of a biological component comprising the step of administering a diagnostically effective amount of a contrast agent according to any one of claims 1, 37, 45, 53 or 61.

98. A method for ultraviolet/visible/ infrared light imaging of a biological component comprising the step of administering a diagnostically effective amount of a contrast agent according to any one of claims 1, 37, 45, 53 or 61.

99. A pharmaceutical composition comprising a contrast agent according to any one of claims 1, 37, 45, 53 or 61 and a carrier, adjuvant or vehicle.

100. The pharmaceutical composition according to claim 99, further comprising a free organic ligand or a pharmaceutically acceptable salt thereof.

101. The pharmaceutical composition according to claim 99, further comprising a free organic ligand or calcium, sodium, meglumine or combination salts thereof.

102. A method of administering a contrast agent according to any one of claims 1, 37, 45, 53 or 61, comprising the steps of:

a) withdrawing a patient's blood into a syringe that contains the contrast agent;

b) mixing the blood and contrast agent in the syringe;

c) and reinjecting the mixture into the patient.